IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of)
)
Pierre DRUILHE)
) Group Art Unit: 1645
Serial No.:10/774,602)
) Examiner: N.M. Minnifield
Filed: February 10, 2004)
)

For: PLASMODIUM FALCIPARUM ANTIGENS INDUCING PROTECTIVE ANTIBODIES

1.132 DECLARATION

Hon. Commissioner of Patents
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I, Pierre Druilhe do hereby declare the following:

[1] I am currently the director of the Biomedical Parasitology Unit at Institut Pasteur in Paris, France and have been the director of this department for many years. I have published 260 articles and have 10 U.S. Patents issued in my name. I am one of the inventors of the above-captioned U.S. patent application. Enclosed please find attached a copy of my *Curriculum Vitae*.

[2] I have read the last U.S. Official Action dated March 25, 2005, for the above-identified patent application. It is my understanding that the Examiner deems that the claims directed to vaccines cannot be produced by a scientist using the disclosure of the above-captioned specification since the specification does not teach a scientist how to obtain a malaria vaccine. It appears that the Examiner's reasoning in

maintaining this rejection is that she deems that none of the claimed peptides either alone or in combination will protect against malaria. I respectfully disagree with the Examiner for the following reasons.

[3] MSP-3 is a polymorphic protein that binds to the merozoite surface and traffics to the parasitophorous vacuole. It has a molecular weight of 48 KD and is recognized by cytophilic antibodies IgG1 and IgG3 in protected subjects and non-cytophilic antibodies in unprotected subjects. This protein is further capable of inducing antibodies which cooperate with monocytes in the antibody-dependent cellular inhibition (ADCI) reaction. Within this protein, certain conformational epitopes are recognized by T lymphocytes. The present specification provides long synthetic peptides which have particular conformational epitopes recognized by T lymphocytes and B epitopes such as MSP-3a, MSP-3b, MSP-3c and MSP-3d. Furthermore, IFN-γ secretion in response to the LSP peptide was extremely high in the range of 10,000 to 50,000 International Units and remained high over the immunization process.

[4] Besides the overview presented above in paragraph (3), the present specification describes the isolation of the clone DG210. The characterization of the protein synthesized by this clone such as inducing an ADCI reaction *in vivo,* the study of lymphoproliferative responses, the sequencing and characterization of the genome clone, and the isotypic characteristics ; i.e., the protein is recognized preferentially by IgG1 and IgG3 in the blood of protected subjects is also described in the present invention.

[5] The study of the polymorphism of the gene and epitopes defined by the clone DG210 was also undertaken using two cultures of strains of African *P.falciprum*, of 4 Thai isolates and 29 African isolates. Screening by Western blot with 6 Thai or African isolates and indirect immunofluorescence of 10 isolates from the Congo confirmed that the epitopes are representative of non-polymorphic conserved regions. The results of these studies were also described in the specification.

[6] A phase I clinical study using a long synthetic peptide derived from MSP3 to evaluate the safety and tolerance of the vaccine, as well as the immunogenicity was disclosed in the specification. In this regard, 36 Swiss volunteers were administered

the synthetic peptide from MSP-3 with either Alum or Montanide® as an adjuvant. The long Synthetic Peptide formulation of MSP-3 was found to be safe and immunogenic. The antibodies that were induced were IgG1 and IgG3, which subclasses of antibodies bind to the Fc gamma receptors on monocytes, thus indicating the monocyte-dependent, antibody-mediated effect.

[7] Additional studies set forth in the specification show natural passive transfer of antibodies from mother to newborns, of IgG3 antibodies and that IgG anti MSP-3b antibodies strongly differentiated 2 groups. Studies were also undertaken in cerebral malaria patients. It should be recalled that cerebral malaria involves the clinical manifestations of *Plasmodium falciparum* malaria that induces mental status and coma. It is a disease of the brain that is accompanied by fever and has a 25% to 50% mortality rate. Ring-like lesions in the brain are major characteristics of this etiology.

[8] The results of a study in Niakhar with 4,200 children, which were sampled during the non-transmission season and followed during the transmission season was also described in the specification. 51 children acquired cerebral malaria, 9 of which died despite treatment. The 9 children that died had significantly lower titers of anti-MSP-3 antibodies compared with the 42 cerebral malaria children who survived and as further compared with 100 acute uncomplicated malaria cases. A similar study was conducted on patients in a hospital of Dakar except serum was taken upon admission. A significant difference was found in IgG3 antimalarial antibodies between survivors and individuals who passed away; i.e., lower titers of anti MSP-3 antibodies were found in those patients who passed away.

[9] Finally the specification discloses a SCID mouse model infected with *P. falciparum* and shows passive transfer in SCID mice.

[10] Besides, the disclosure in the specification additional studies were undertaken since the patent application was filed. The association of MSP-3 antibodies with protection against malaria was demonstrated in Dielmo with over 2 years of follow-up. In the Dielmo studies over 220 individuals of all ages were followed, as well as 62 pregnancies. Daily medical exams were given and sequential sera were taken (at least 88,000 sera samples) preceding a given malaria attack. It was also

demonstrated in Burma in an hyperendemic area and by immunization and challenge of Aotus monkeys.

[11] In fact, additional Western blots, and SGI% of the volunteers which were previously injected with 3 doses of MSP-3 long synthetic peptides in comparison with P1AG were taken after 1 year. Further measurements were made greater than 1 year after immunization of the MSP-3 LSP's of the present invention. The results of the firsts study are indicated in attached Annex I. As can be seen from these results and our further results of greater than one year, the immune response obtained after immunization was long-lasting. Furthermore, biological assays demonstrated that the induced antibodies can mediate protection against *P. falciparum*.

[12] Further results were undertaken in a volunteer that was Western blot positive and administered the MSP-3 LSP's of the present invention. As can be seen in enclosed Annex II, after 12 months post immunization, the parasitemia dropped to 0.01 % on day 30.

[13] Thus, in view of paragraphs [2] to [12] above, the conclusions that can be made are the following:

(a) that MSP3-LSP's set forth in the present invention provide a malaria vaccine that is safe, well tolerated when adjuvated with alum or Montanide® and are able to elicit antibodies in humans that are able to kill *P. falciparum;*

(b) even low doses of MSP3 LSP's injected with simple adjuvants induce long-lasting antibodies of the cytophilic classes;

(c) the MSP3 LSP's of the present invention are directed to fully conserved epitopes and have a strong biological effect against *P. falciparum*; and

(d) the antibodies elicited in volunteers, after injection of the MSP-3 long synthetic proteins of the present invention, were able to inhibit parasite growth both *in vivo* and *in vitro* via the antibody-dependent monocyte-mediated mechanism.

[14] It appears that the Examiner has taken a strict interpretation of the word "vaccine" since at page 7 of the Official Action, the Examiner states that "none of these are clearly indicative that the claimed peptides either alone or in combination will protect against malaria. An immune response is not protection against malaria."

However, it is well known by scientists in this field that the goal of erythrocytic malaria vaccines is either to reduce the parasite load by preventing invasion of red cells or to prevent parasite replication and/or growth after invasion of the parasite. In this regard the present invention provides a mechanism to block the *P. falciparum* parasite as demonstrated in the specification. Thus the result of the ADCI experiments, which is a mechanism mediated by soluble components released by monocytes that block the division of intraerythrocytic parasites, is a clear indication of parasite killing. Indeed, ADCI can provide a means of generating cross-strain protection, since macrophages activated by antibodies to one variant can kill parasites in red blood cells of other strains and variants of *P. falciparum*. Moreover ADCI can continue after merozoite invasion and entry into the red blood cells.

[15] In view of paragraphs [1] to [14], it can only be concluded that a scientist in this field can gather from the contents of the specification that malaria vaccines can be produced by a scientist using the disclosure of the above-captioned specification

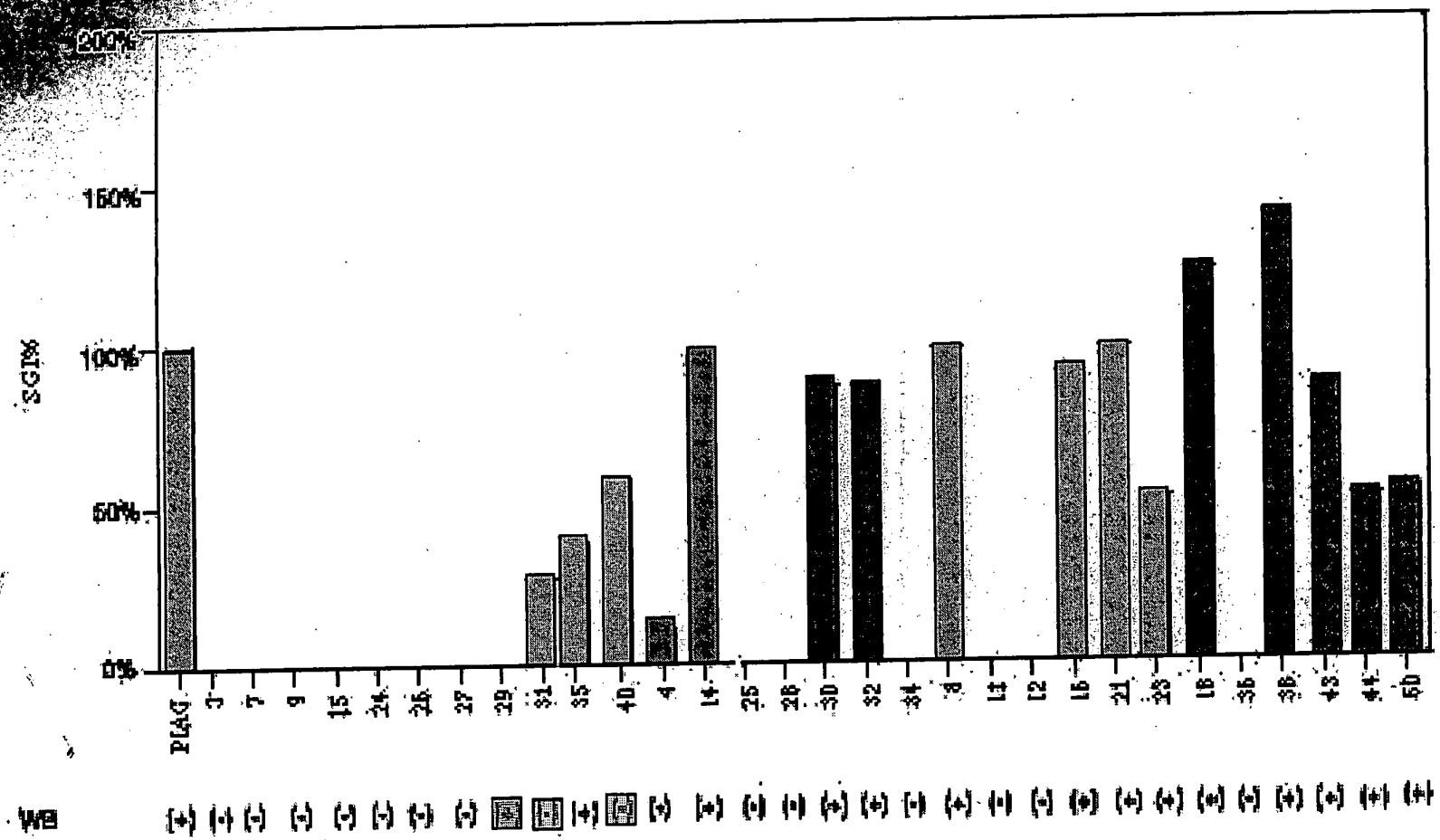
I also declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

27-05-2005

Date

Pierre DRUILHE

Western blot result and SGI% of the volunteers one year after 3 doses of MSP3 Long Synthetic Peptide immunization in comparison with P1AG.



: M 10-10-10 (6)

: M 20-20-20 (5)

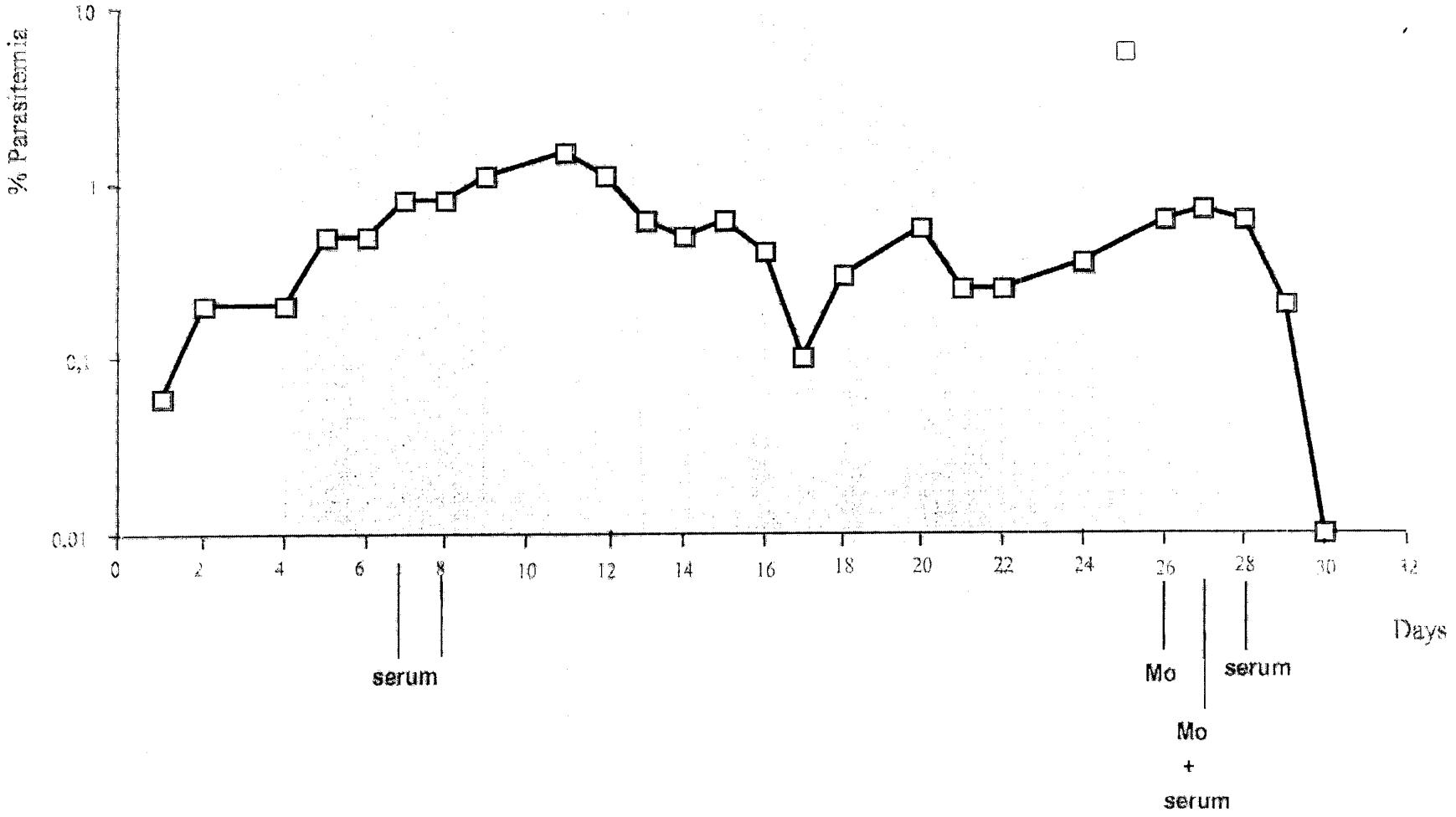
: M 30-30-10 (4)

: M 100-10-10 (3)

: A 30-30-30 (6)

: A 100-10-10 (6)

Volonteer 18, 12 months post-immunisation, WB+



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1972 - Medical Degree, Paris University
1972 - Post-graduate degree in Haematology (University of Paris)
1972 - Post-graduate degree in Medical Parasitology (University of Paris)
1975 - Post-graduate degree in Immunology (University of Paris)

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Ss-Dossier **224531 FR 01 ANTIG. HEPATIQUE P FALCIPARUM** Inventeur: **DRU002 DRUILHE PIERRE**
N° D.I 186028 ANTIGENES HEPATIQUE DE P. FALCIPARUM

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
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224531 AT 01	AUTRICHE	EU889018545	9/02/1988		INSTITUT PASTEUR	CNRS	
224531 AU 01	AUSTRALIE	AU1342888	9/02/1988		INSTITUT PASTEUR	CNRS	
224531 BE 01	BELGIQUE	EU889018545	9/02/1988		INSTITUT PASTEUR	CNRS	
224531 CH 01	SUISSE	EU889018545	9/02/1988		INSTITUT PASTEUR	CNRS	
224531 DE 01	ALLEMAGNE	EU889018545	9/02/1988		INSTITUT PASTEUR	CNRS	
224531 EP 01	DEP.EUROP.	EU889018545	9/02/1988		INSTITUT PASTEUR	CNRS	
224531 FR 02	FRANCE	EU889018545	9/02/1988		INSTITUT PASTEUR	CNRS	
224531 GB 01	GR.BRETAG.	EU889018545	9/02/1988		INSTITUT PASTEUR	CNRS	
224531 IT 01	ITALIE	EU889018545	9/02/1988		INSTITUT PASTEUR	CNRS	
224531 JP 01	JAPON	JP501827	9/02/1988		INSTITUT PASTEUR	CNRS	
224531 LI 01	LIECHTENST	EU889018545	9/02/1988		INSTITUT PASTEUR	CNRS	
224531 LU 01	LUXEMBOURG	EU889018545	9/02/1988		INSTITUT PASTEUR	CNRS	
224531 PC 01	PCT	PCTFR8800074	9/02/1988		INSTITUT PASTEUR	P.M.S.V.	CNRS
224531 US 01	ETATS-UNIS	US275139	9/02/1988		INSTITUT PASTEUR	CNRS	
224531 US 02	ETATS-UNIS	US462512	7/06/1995	Division	INSTITUT PASTEUR	CNRS	
224531 US 03	ETATS-UNIS	US462062	7/06/1995	Division	INSTITUT PASTEUR	CNRS	
224531 US 04	ETATS-UNIS	US760000	3/12/1996	Division	INSTITUT PASTEUR	CNRS	

Ss-Dossier **224532 FR 01 ANTIGENE SPOROZOITE-HEPATIQUE** Inventeur: **DRU002 DRUILHE PIERRE**
N° D.I 189011 ANTIGENES DE SPOROZOITE DE P.FALCIPARUM

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
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224532 AU 01	AUSTRALIE	AU5315790	11/04/1990		INSTITUT PASTEUR	CNRS	
224532 EP 01	DEP.EUROP.	EU904009859	10/04/1990		INSTITUT PASTEUR	CNRS	
224532 NZ 01	NVL.ZELAND	NZ233328	12/04/1990		INSTITUT PASTEUR	CNRS	
224532 PT 01	PORTUGAL	PT93764	12/04/1990		INSTITUT PASTEUR	CNRS	
224532 US 01	ETATS-UNIS	US507215	11/04/1990		INSTITUT PASTEUR	CNRS	
224532 US 02	ETATS-UNIS	US758724	9/09/1991	Contin° in Part	INSTITUT PASTEUR	CNRS	
224532 US 03	ETATS-UNIS	US104597	10/08/1993		INSTITUT PASTEUR	CNRS	
224532 US 04	ETATS-UNIS	US242060	13/05/1994	Contin° in Part	INSTITUT PASTEUR	CNRS	
224532 US 05	ETATS-UNIS	US837098	14/04/1997	Division	INSTITUT PASTEUR	CNRS	
224532 US 06	ETATS-UNIS	US EN ATTENTE	18/03/1999	Continuation	INSTITUT PASTEUR	CNRS	
224532 ZA 01	AFRQ-SUD	ZA902831	12/04/1990		INSTITUT PASTEUR	CNRS	

Ss-Dossier **233621 FR 01 EPITOPE T DE P. FALCIPARUM** Inventeur: **DRU002 DRUILHE PIERRE**
N° D.I 190014 EPITOPE T DE P. FALCIPARUM

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
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233621 AT 01	AUTRICHE	EU929058972	5/02/1992		INSTITUT PASTEUR	CNRS	
233621 BE 01	BELGIQUE	EU929058972	5/02/1992		INSTITUT PASTEUR	CNRS	
233621 CA 01	CANADA	CA2101924	5/02/1992		INSTITUT PASTEUR	CNRS	
233621 CH 01	SUISSE	EU929058972	5/02/1992		INSTITUT PASTEUR	CNRS	
233621 DE 01	ALLEMAGNE	EU929058972	5/02/1992		INSTITUT PASTEUR	CNRS	
233621 DK 01	DANEMARK	EU929058972	5/02/1992		INSTITUT PASTEUR	CNRS	
233621 EP 01	DEP.EUROP.	EU929058972	5/02/1992		INSTITUT PASTEUR	CNRS	
233621 ES 01	ESPAGNE	EU929058972	5/02/1992		INSTITUT PASTEUR	CNRS	
233621 FR 02	FRANCE	EU929058972	5/02/1992		INSTITUT PASTEUR	CNRS	
233621 GB 01	GR.BRETAG.	EU929058972	5/02/1992		INSTITUT PASTEUR	CNRS	
233621 GR 01	GRECE	EU929058972	5/02/1992		INSTITUT PASTEUR	CNRS	
233621 IT 01	ITALIE	EU929058972	5/02/1992		INSTITUT PASTEUR	CNRS	
233621 JP 01	JAPON	PCTFR9200104	5/02/1992		INSTITUT PASTEUR		

233621	LI	01	LIECHTENST	EU929058972	5/02/1992		INSTITUT PASTEUR	CNRS
233621	LU	01	LUXEMBOURG	EU929058972	5/02/1992		INSTITUT PASTEUR	CNRS
233621	MC	01	MONACO	EU929058972	5/02/1992		INSTITUT PASTEUR	CNRS
233621	NL	01	PAYS-BAS	EU929058972	5/02/1992		INSTITUT PASTEUR	CNRS
233621	PC	01	PCT	PCTFR9200104	5/02/1992		INSTITUT PASTEUR	
233621	SE	01	SUEDE	EU929058972	5/02/1992		INSTITUT PASTEUR	CNRS
233621	US	01	ETATS-UNIS	US098327	5/02/1992		INSTITUT PASTEUR	CNRS
233621	US	02	ETATS-UNIS	US462625	7/06/1995	Division	INSTITUT PASTEUR	CNRS
233621	US	03	ETATS-UNIS	US837344	19/04/2001	Division	INSTITUT PASTEUR	CNRS
233621	US	04	ETATS-UNIS	US900963	10/07/2001	Division	INSTITUT PASTEUR	CNRS

Ss-Dossier 250068 FR 01 P48KD DE P. FALCIPARUM Inventeur: **DRU002 DRUILHE PIERRE**

N° D.I 192053 P48KD DE P. FALCIPARUM

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
250068	AT 01 AUTRICHE	EU939235842	18/10/1993		INSTITUT PASTEUR		
250068	BE 01 BELGIQUE	EU939235842	18/10/1993		INSTITUT PASTEUR		
250068	CH 01 SUISSE	EU939235842	18/10/1993		INSTITUT PASTEUR		
250068	DE 01 ALLEMAGNE	EU939235842	18/10/1993		INSTITUT PASTEUR		
250068	DK 01 DANEMARK	EU939235842	18/10/1993		INSTITUT PASTEUR		
250068	EP 01 DEP.EUROP.	EU939235842	18/10/1993		INSTITUT PASTEUR		
250068	EP 02 DEP.EUROP.	EU040039455	18/10/1993	Division	INSTITUT PASTEUR		
250068	ES 01 ESPAGNE	EU939235842	18/10/1993		INSTITUT PASTEUR		
250068	FR 02 FRANCE	EU939235842	18/10/1993		INSTITUT PASTEUR		
250068	GB 01 GR.BRETAG.	EU939235842	18/10/1993		INSTITUT PASTEUR		
250068	GR 01 GRECE	EU939235842	18/10/1993		INSTITUT PASTEUR		
250068	IE 01 IRLANDE	EU939235842	18/10/1993		INSTITUT PASTEUR		
250068	IT 01 ITALIE	EU939235842	18/10/1993		INSTITUT PASTEUR		
250068	JP 01 JAPON	PCTFR9301024	18/10/1993		INSTITUT PASTEUR		
250068	LI 01 LIECHTENST	EU939235842	18/10/1993		INSTITUT PASTEUR		
250068	LU 01 LUXEMBOURG	EU939235842	18/10/1993		INSTITUT PASTEUR		
250068	MC 01 MONACO	EU939235842	18/10/1993		INSTITUT PASTEUR		
250068	NL 01 PAYS-BAS	EU939235842	18/10/1993		INSTITUT PASTEUR		
250068	PC 01 PCT	PCTFR9301024	18/10/1993		INSTITUT PASTEUR		
250068	PT 01 PORTUGAL	EU939235842	18/10/1993		INSTITUT PASTEUR		
250068	SE 01 SUEDE	EU939235842	18/10/1993		INSTITUT PASTEUR		
250068	US 01 ETATS-UNIS	US416711	18/10/1993		INSTITUT PASTEUR		
250068	US 02 ETATS-UNIS	US356497	19/07/1999	Division	INSTITUT PASTEUR		
250068	US 03 ETATS-UNIS	US238741	11/09/2002	Continuation	INSTITUT PASTEUR		
250068	US 04 ETATS-UNIS	US294770	15/11/2002	Continuation	INSTITUT PASTEUR		
250068	US 05 ETATS-UNIS	US774602	10/02/2004	Continuation	INSTITUT PASTEUR		

Ss-Dossier 250136 FR 01 AG LSA3 DE P. FALCIPARUM Inventeur: **DRU002 DRUILHE PIERRE**

N° D.I 194054 AG LSA3 DE P. FALCIPARUM

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
250136	AU 01 AUSTRALIE	AU6309696	12/06/1996		INSTITUT PASTEUR		
250136	CA 01 CANADA	CA2221029	12/06/1996		INSTITUT PASTEUR		
250136	EP 01 DEP.EUROP.	EU969221076	12/06/1996		INSTITUT PASTEUR		
250136	JP 01 JAPON	JP5027119794	12/06/1996		INSTITUT PASTEUR		
250136	PC 01 PCT	PCTFR9600894	12/06/1996		INSTITUT PASTEUR		
250136	US 01 ETATS-UNIS	US973462	12/06/1996		INSTITUT PASTEUR		
250136	US 02 ETATS-UNIS	US742096	20/12/2000	Division	INSTITUT PASTEUR		

Ss-Dossier 250260 US 01 COMPOSES LIPIDO-PEPTIDIQUES Inventeur: **DRU002 DRUILHE PIERRE**

N° D.I 199044 COMPOSES LIPIDO-PEPTIDIQUES

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
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250260 AL 01	ALBANIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 AU 01	AUSTRALIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 BB 01	BARBADE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 BG 01	BULGARIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 BO 01	BOLIVIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 BR 01	BRESIL	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 BU 01	BIRMANIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 BY 01	BELARUS	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 CA 01	CANADA	CA2390747	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 CN 01	CHINE POP.	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 CS 01	TCHECOSLOV	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 CU 01	CUBA	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 EP 01	DEP.EUROP.	EU009919747	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 GE 01	GEORGIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 GH 01	GHANA	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 HU 01	HONGRIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 ID 01	INDONESIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 IL 01	ISRAEL	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 IN 01	INDE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 IS 01	ISLANDE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 JP 01	JAPON	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 KE 01	KENYA	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 KP 01	COREE NORD	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 KR 01	COREE SUD	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 KZ 01	KAZACKSTAN	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 MA 01	MAROC	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 MG 01	MADAGASCAR	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 MX 01	MEXIQUE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 MY 01	MALAISIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 NZ 01	NVL.ZELAND	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 OA 01	O.A.P.I.	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 PC 01	PCT	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 PH 01	PHILIPPINE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 PL 01	POLOGNE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 RO 01	ROUMANIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 SG 01	SINGAPOUR	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 SK 01	SARAWAK	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 SL 01	SIER.LEONE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 SQ 01	SLOVAQUIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 SU 01	FED RUSSIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 TH 01	THAILANDE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 TK 01	TRANSKEI	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 TR 01	TURQUIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 US 03	ETATS-UNIS	US161760	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 VN 01	VIET-NAM	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 YU 01	CROATIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 ZA 01	AFRQ-SUD	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	

Ss-Dossier 250260 US 02 COMPOSES LIPIDO-PEPTIDIQUES Inventeur: **DRU002 DRUILHE PIERRE**

N° D.I 199044 COMPOSES LIPIDO-PEPTIDIQUES

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
------- -- --	ETATS-UNIS	US732754	11/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	

Ss-Dossier 250260 US 04 COMPOSES LIPIDO-PEPTIDIQUES Inventeur: **DRU002 DRUILHE PIERRE**

N° D.I 199044 COMPOSES LIPIDO-PEPTIDIQUES

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
------- -- --	ETATS-UNIS	US206535	29/07/2002	Division	INSTITUT PASTEUR	UNIVERSITE DE LIL	

Ss-Dossier 250300 EP 01 LSA 3 et adjuvants Inventeur: **DRU002 DRUILHE PIERRE**

N° D.I 200064 LSA 3 et adjuvants

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
------- -- --	DEP.EUROP.	EU002037240	25/10/2000		INSTITUT PASTEUR	SMITH KLINE BEECH	
250300 CA 01	CANADA	PCTEP0112349	23/10/2001		INSTITUT PASTEUR	SMITH KLINE BEECH	
250300 EP 02	DEP.EUROP.	EU019903749	23/10/2001		INSTITUT PASTEUR	SMITH KLINE BEECH	
250300 JP 01	JAPON	JP202540758	23/10/2001		INSTITUT PASTEUR	SMITH KLINE BEECH	
250300 PC 01	PCT	PCTEP0112349	23/10/2001		INSTITUT PASTEUR	SMITH KLINE BEECH	
250300 US 01	ETATS-UNIS	PCTEP0112349	23/10/2001		INSTITUT PASTEUR	SMITH KLINE BEECH	

Ss-Dossier 250322 CA 01 Antigènes de Plasmodium falciparum Inventeur: **DRU002 DRUILHE PIERRE**

N° D.I 201031 Antigènes de Plasmodium falciparum

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
------- -- --	CANADA	CA2345206	16/05/2001		INSTITUT PASTEUR		
250322 AL 01	ALBANIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 AU 01	AUSTRALIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 BB 01	BARBADE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 BG 01	BULGARIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 BO 01	BOLIVIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 BR 01	BRESIL	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 BU 01	BIRMANIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 BY 01	BELARUS	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 CA 03	CANADA	CA2382977	15/05/2002		INSTITUT PASTEUR		
250322 CN 01	CHINE POP.	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 CS 01	TCHECOSLOV	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 CU 01	CUBA	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 EP 01	DEP.EUROP.	EU027328723	15/05/2002		INSTITUT PASTEUR		
250322 GE 01	GEORGIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 GH 01	GHANA	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 HU 01	HONGRIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 ID 01	INDONESIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 IL 01	ISRAEL	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 IN 01	INDE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 IS 01	ISLANDE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 JP 01	JAPON	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 KE 01	KENYA	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 KP 01	COREE NORD	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 KR 01	COREE SUD	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 KZ 01	KAZACKSTAN	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 MA 01	MAROC	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 MG 01	MADAGASCAR	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 MX 01	MEXIQUE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 MY 01	MALAISIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 NZ 01	NVL.ZELAND	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 OA 01	O.A.P.I.	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 PC 01	PCT	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 PH 01	PHILIPPINE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 PL 01	POLOGNE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 RO 01	ROUMANIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 SG 01	SINGAPOUR	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 SK 01	SARAWAK	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322 SL 01	SIER.LEONE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		

250322	SQ	01	SLOVAQUIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR
250322	SU	01	FED RUSSIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR
250322	TH	01	THAILANDE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR
250322	TK	01	TRANSKEI	PCTFR0201637	15/05/2002		INSTITUT PASTEUR
250322	TN	01	TUNISIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR
250322	TR	01	TURQUIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR
250322	US	01	ETATS-UNIS	US712533	15/05/2002		INSTITUT PASTEUR
250322	VN	01	VIET-NAM	PCTFR0201637	15/05/2002		INSTITUT PASTEUR
250322	YU	01	CROATIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR
250322	ZA	01	AFRQ-SUD	PCTFR0201637	15/05/2002		INSTITUT PASTEUR

Ss-Dossier **250322 CA 02 Antigènes de Plasmodium falciparum** Inventeur: **DRU002 DRUILHE PIERRE**

, N° D.I 201031 Antigènes de Plasmodium falciparum

N° Ss-Dossier			Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
250322	AL	01	ALBANIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	AU	01	AUSTRALIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	BB	01	BARBADE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	BG	01	BULGARIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	BO	01	BOLIVIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	BR	01	BRESIL	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	BU	01	BIRMANIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	BY	01	BELARUS	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	CA	03	CANADA	CA2382977	15/05/2002		INSTITUT PASTEUR		
250322	CN	01	CHINE POP.	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	CS	01	TCHECOSLOV	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	CU	01	CUBA	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	EP	01	DEP.EUROP.	EU027328723	15/05/2002		INSTITUT PASTEUR		
250322	GE	01	GEORGIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	GH	01	GHANA	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	HU	01	HONGRIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	ID	01	INDONESIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	IL	01	ISRAEL	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	IN	01	INDE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	IS	01	ISLANDE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	JP	01	JAPON	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	KE	01	KENYA	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	KP	01	COREE NORD	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	KR	01	COREE SUD	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	KZ	01	KAZACKSTAN	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	MA	01	MAROC	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	MG	01	MADAGASCAR	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	MX	01	MEXIQUE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	MY	01	MALAISIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	NZ	01	NVL.ZELAND	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	OA	01	O.A.P.I.	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	PC	01	PCT	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	PH	01	PHILIPPINE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	PL	01	POLOGNE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	RO	01	ROUMANIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	SG	01	SINGAPOUR	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	SK	01	SARAWAK	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	SL	01	SIER.LEONE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	SQ	01	SLOVAQUIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	SU	01	FED RUSSIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		
250322	TH	01	THAILANDE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR		

250322 TK 01 TRANSKEI	PCTFR0201637	15/05/2002		INSTITUT PASTEUR	
250322 TN 01 TUNISIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR	
250322 TR 01 TURQUIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR	
250322 US 01 ETATS-UNIS	US712533	15/05/2002		INSTITUT PASTEUR	
250322 VN 01 VIET-NAM	PCTFR0201637	15/05/2002		INSTITUT PASTEUR	
250322 YU 01 CROATIE	PCTFR0201637	15/05/2002		INSTITUT PASTEUR	
250322 ZA 01 AFRQ-SUD	PCTFR0201637	15/05/2002		INSTITUT PASTEUR	

Ss-Dossier **250322 CA 04 Antigènes de Plasmodium falciparum** Inventeur: **DRU002 DRUILHE PIERRE**

N° D.I 201031 Antigènes de Plasmodium falciparum

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
------- -- --	CANADA	CA2382977	15/05/2002		INSTITUT PASTEUR		

Ss-Dossier **250369 GB 01 Anticorps recombinants de P.falciparum** Inventeur: **DRU002 DRUILHE PIERRE**

N° D.I 202046 Anticorps recombinants de P.falciparum

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
------- -- --	GR.BRETAG.	GB010200575	16/08/2001		DANISH TECHNOLOGI	INSTITUT PASTEUR	
250369 AU 01	AUSTRALIE	AU2002326106	16/08/2002		DANISH TECHNOLOGI	INSTITUT PASTEUR	
250369 BR 01	BRESIL	BR02119439	16/08/2002		DANISH TECHNOLOGI	INSTITUT PASTEUR	
250369 CA 01	CANADA	CA2458890	16/08/2002		DANISH TECHNOLOGI	INSTITUT PASTEUR	
250369 EP 01	DEP.EUROP.	EU027605138	16/08/2002		DANISH TECHNOLOGI	INSTITUT PASTEUR	
250369 JP 01	JAPON	JP2003-521275	16/08/2002		DANISH TECHNOLOGI	INSTITUT PASTEUR	
250369 PC 01	PCT	PCTIB0203995	16/08/2002		DANISH TECHNOLOGI	INSTITUT PASTEUR	
250369 US 01	ETATS-UNIS	US486703	16/08/2002		DANISH TECHNOLOGI	INSTITUT PASTEUR	

Ss-Dossier **250381 US 01 Composition immunogène dérivée de RSP3** Inventeur: **DRU002 DRUILHE PIERRE**

N° D.I 202101 Composition immunogène dérivée de RSP3

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
------- -- --	ETATS-UNIS	US294770	15/11/2002	Contin° in Part	INSTITUT PASTEUR		

Ss-Dossier **250424 EP 01 Antibodies effective at killing P.falci** Inventeur: **DRU002 DRUILHE PIERRE**

N° D.I 203044 Antibodies effective at killing P.falci.

N° D.I 202101 Composition immunogène dérivée de RSP3

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
------- -- --	DEP.EUROP.	EP032926735	24/10/2003		INSTITUT PASTEUR		
250424 PC 01	PCT	PCTEP2004012909	22/10/2004		INSTITUT PASTEUR		

Ss-Dossier **250426 US 01 MSP-3 GLURP malaria vaccine candidate** Inventeur: **DRU002 DRUILHE PIERRE**

N° D.I 203080 MSP-3 GLURP malaria vaccine candidate

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
------- -- --	ETATS-UNIS	US691672	24/10/2003		INSTITUT PASTEUR		
250426 PC 01	PCT	PCTEP2004012910	22/10/2004		INSTITUT PASTEUR		

Ss-Dossier **250431 EP 01 Nouvel antigène de P.falciparum : LSA-5** Inventeur: **DRU002 DRUILHE PIERRE**

N° D.I 203034 Nouvel antigène de P.falciparum : LSA-5

N° D.I 202121 Nouvel antigène de P.falciparum : LSA-5

N° D.I 202006B Nouvel Antigene de P.falciparum

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
------- -- --	DEP.EUROP.	EU032931586	15/12/2003		INSTITUT PASTEUR		

Ss-Dossier **250431 PC 01 Nouvel antigène de P.falciparum : LSA-5** Inventeur: **DRU002 DRUILHE PIERRE**

N° D.I 203034 Nouvel antigène de P.falciparum : LSA-5

N° D.I 202121 Nouvel antigène de P.falciparum : LSA-5

N° D.I 202006B Nouvel Antigene de P.falciparum

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
------- -- --	PCT	PCTEP2004014848	15/12/2004		INSTITUT PASTEUR		

Ss-Dossier **250435 EP 01 Modèle souris** Inventeur: **DRU002 DRUILHE PIERRE**
N° D.I 203134 Development of an improved mouse model

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
------- -- --	DEP.EUROP.	EU042900662	9/01/2004		INSTITUT PASTEUR		
250435 PC 01	PCT	PCTEP2005000547	7/01/2005		INSTITUT PASTEUR		

Ss-Dossier **250453 EP 01 Major improvement in human hepatocytes** Inventeur: **DRU002 DRUILHE PIERRE**
N° D.I 203100 Major improvement in human hepatocytes

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
------- -- --	DEP.EUROP.	EU042900654	9/01/2004		INSTITUT PASTEUR	INSERM	
250453 PC 01	PCT	PCTEP2005000546	7/01/2005		INSTITUT PASTEUR	INSERM	

Ss-Dossier **250458 US 01 Antibodies against malaria** Inventeur: **DRU002 DRUILHE PIERRE**
N° D.I 204076 Antibodies against malaria

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
------- -- --	ETATS-UNIS	US598062	2/08/2004		INSTITUT PASTEUR		

** Fin d'Edition **